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Short Communication

Measles in Italy: Viral strains and crossing borders

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ABSTRACT

In 2017, Italy experienced one of the largest outbreaks of measles in recent years, with 5404 notified cases and 4347 confirmed cases. A further 2029 cases were notified during the first 6 months of 2018, and 1516 of them were laboratory-confirmed. The B3 and D8 genotypes were identified as those responsible for the outbreak. Possible transmission routes can be established by monitoring the circulating measles virus strains in support of the national health authorities to warn people and travellers.

After the large epidemic of measles in 2017, with 5404 notified cases and 4347 confirmed cases, between January 1 and June 30, 2018, 2029 cases of measles were reported to the Italian national measles and rubella surveillance system. Of these, 1516 (75%) were laboratory-confirmed in accordance with the World Health Organization (WHO) guidelines, as described previously (Istituto Superiore di Sanità (ISS), 2018a; Magurano et al., 2015). The outbreak reached its peak in the month of April 2018, with 466 cases (Figure 1), and showed slight signs of a turnaround at the time of writing this article.

Among 2029 notified cases, 1516 (74.7%) were laboratory-confirmed in accordance with the WHO guidelines, by molecular ($n = 540$) or serological methods ($n = 976$), at the National Reference Laboratory (Magurano et al., 2015) and the Network of Italian Reference Laboratories for Measles and Rubella (MoRoNet) (Istituto Superiore di Sanità (ISS), 2018b). Among the PCR-positive samples, 338 sequences were obtained by amplifying a fragment of the carboxyl-terminal coding region of the N gene, including the 450-bp fragment recommended for genotyping (Magurano et al., 2015; World Health Organization, 2012a), and were analysed phylogenetically. All sequences were submitted to the Measles Nucleotide Surveillance (MeaNS) database (Rota et al., 2011).

The analysis of the sequences identified in Italy during the first half of 2018 demonstrated the co-circulation of genotypes B3 and D8, with 272 and 66 sequences identified, respectively.

BLAST analysis in MeaNS established that among the sequences belonging to genotype B3, 157 were identical to the WHO named strain MVs/Dublin.IRL/8.16, also responsible for several outbreaks in Europe. MVs/Dublin.IRL/8.16 has been circulating in Italy since 2017. Evidence of the introduction of this strain to Italy dates back to the end of 2016, and it occurred as a result of several importations in Northern Italy from Romania, as supported by epidemiological data. Fifty-nine B3 sequences were identical to the WHO strain MVs/SaintDenis.FRA/36.17/. This strain has been circulating in Italy since 2017, but there are no epidemiological data to support the hypothesis of importation from abroad. Ten sequences were identical to the WHO strain MVs/Ljubljana.SVN/27.17/. Evidence of importation from the Czech Republic was provided for nine of these sequences.

Beyond these variants, the remaining 46 sequences classified as B3, but not identical to any of the WHO strains, were closely related to the B3 strains included in Figure 2: 20 were closely related to strain MVs/Dublin.IRL/8.16, one to MVs/SaintDenis.FRA/36.17, eight to MVs/Islamabad.PAK/1.13/, and 17 to MVs/Kabul.AFG/20.2014/3. For several of these cases, evidence of importation was

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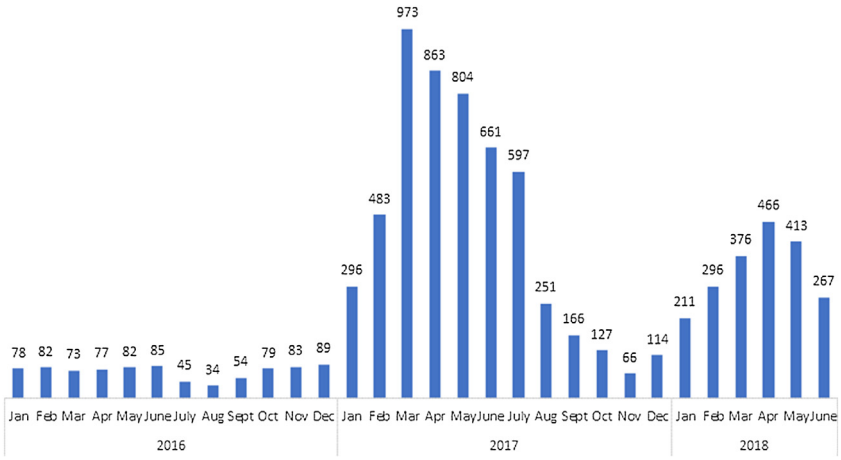

Figure 1. Reported measles cases by month of rash onset, Italy, January 2016 – June 2018 (n = 8 291).

established by epidemiological links to cases returning from abroad (countries of origin are reported in Figure 2 in brackets).

Among the 66 sequences belonging to genotype D8, 15 were identical to WHO named strain MVs/GirSomnath.IND/42.16/, nine were identical to MVs/Herborn.DEU/05.17/, three to MVs/Victoria.AUS/6.11/, and four to MVs/Cambridge.GBR/5.16/. The introduction of strain MVs/Herborn.DEU/05.17/into Italy dates back to two importation events. The first event was linked to four patients returning from England (February 2018). The second one was linked to a patient who had travelled in Switzerland (April 2018). The named strain MVs/Victoria.AUS/6.11/was identified in two patients who had travelled in Thailand (May 2018), suggesting the introduction of this strain from the Orient. Named strain MVs/GirSomnath.IND/42.16/was identified in a patient returning from Germany. MVs/Cambridge.GBR/5.16/was identified in two patients returning from Ukraine.

The remaining 35 sequences were not identical to any of the D8 named strains. Twenty-two were closely related to MVs/FrankfurtMain.DEU/17.11, four to MVs/Gadag.IND/02.13, four to MVs/Victoria.AUS/6.11, two to MVs/Thiruvananthapuram.IND/18.12, one to MVs/Herborn.DEU/05.17/, and two to MVs/Cambridge.GBR/5.16/. Evidence of importations was established by epidemiological links to patients returning from abroad (countries of origin are reported in Figure 2 in brackets).

According to the MeaNS database, many European countries have reported the dominance of B3 and D8 measles strains in 2018. Italian epidemiological data indicate that several cases of measles were caused by strains imported to Italy from the Czech Republic, Germany, Switzerland, France, India, and Thailand, as shown in the phylogenetic tree (Figure 2).

Measles is a highly infectious vaccine-preventable disease and is still one of the leading causes of childhood mortality globally. The WHO European Region (WHO/Europe) has adopted the goal of eliminating measles and rubella, but despite the significant progress made towards this goal, the elimination of measles and rubella in the region is yet to be achieved (World Health Organization, 2012b; Datta et al., 2018; Adamo et al., 2017).

According to the latest assessment by the European Regional Verification Commission for Measles and Rubella Elimination (RVC) of June 2018, 43 of the region's 53 member states have interrupted the endemic spread of measles (based on 2017 reporting). The RVC has also stated concern over poor disease surveillance and low immunization coverage in several countries (World Health Organization, 2018a).

Member States of WHO/Europe submit monthly reports on suspected and confirmed measles and rubella cases identified through their national disease surveillance systems to the WHO. Between January 1 and June 31, 2018, 41 013 cases of measles were reported to WHO/Europe or via the European Surveillance System ECDC/TESSy, according to WHO EpiData published on August 1, 2018 (World Health Organization, 2018b). Eighty-four percent of all the cases occurred in Ukraine (23 070), Serbia (4954), France (2579), Greece (2130), and Italy (2029), accounting for 56%, 12%, 6%, 5%, and 5%, respectively.

During the same period, a total of 1748 measles virus sequences were reported by the reference laboratories of the WHO/Europe, according to the MeaNS database as of July 19, 2018. The genotypes identified throughout Europe were B3 ($n = 952$), D8 ($n = 790$), D9 ($n = 5$), and A ($n = 1$). Genotype B3 included several lineages, comprising the more widespread WHO strain MVs/Dublin.IRL/8.16/ and other B3 named strain MVs/SaintDenis.FRA/36.17/. Named strains belonging to genotype D8 were MVs/GirSomnath.IND/42.16/, MVs/Herborn.DEU/05.17/, MVs/Cambridge.GBR/5.16/, MVs/Victoria.AUS/6.11/, and MVs/Hulu Langat.MYS/26.11/.

Virus characterization (by sequencing and information about genotypes) is considered essential to verify the status of measles elimination in Europe. Furthermore, monitoring of named strains with epidemiological information for adequate case classification and characterization of the chains of transmission allows an understanding of the picture of measles circulation. Genetic data describing virus variants represent a key component of the verification of elimination of indigenous measles. It is also an invaluable tool in public health investigations, both to establish whether connections exist between concurrent measles cases and to indicate possible sources of importations from endemic countries, such as Italy.

Epidemiological data from European measles surveillance show that measles is currently endemic in several European countries. The analysis of epidemiological and genetic data from several Italian cases confirms that Italy imported measles from some of these countries (Figure 2). Moreover, data from MeaNS show that the named strain MVs/Dublin.IRL/8.16/ was imported from Italy to Mexico (February 2018) and to the USA (April 2018). This strain was also identified in the UK at the beginning of 2018 in patients returning from Italy. This demonstrates that when unvaccinated individuals travel to endemic countries where outbreaks are ongoing, the cross-border transmission between member states of the same WHO region and between different WHO regions is an

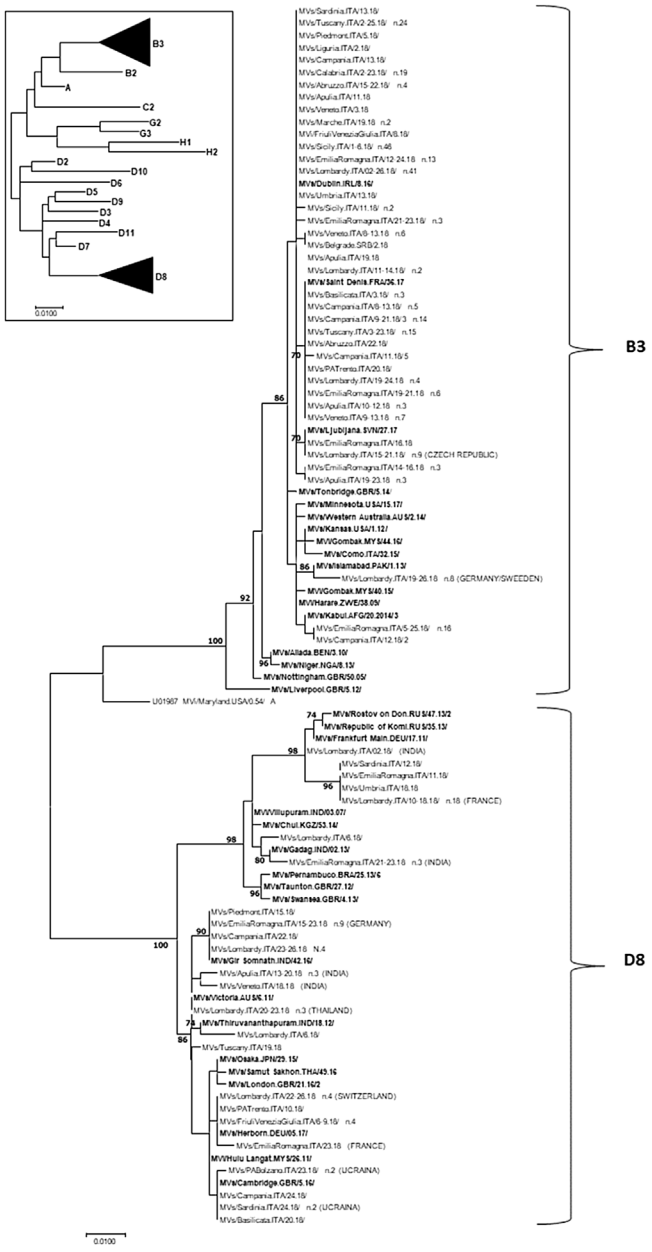

Figure 2. Phylogenetic tree constructed by using the Maximum Likelihood method based on the Kimura 2-parameter model. The evolutionary analyses were conducted in MEGA7. The percentage of trees in which the associated taxa clustered together is shown next to the branches. The tree is drawn to scale, with branch lengths measured in the number of substitutions per site. Number of identical sequences identified in the same province by the same week is reported.

expected event. In this context, the named strains identified in Italy during 2018 can support measles surveillance in countries in the WHO European Region to better identify chains of transmission outside of Italy and monitor the circulation of the virus.

It is important to raise awareness in the population to the fact that measles is circulating in various European countries and to encourage people to check their measles vaccination status, particularly before travelling abroad, especially in the summer when the number of people travelling increases.

Two doses of measles-containing vaccine are 97% effective against measles. The target immunization coverage set by the WHO for the second dose of measles-containing vaccine is 95%; however, 20 of 27 European countries have rates below that level, including Italy (World Health Organization, 2017). European travellers should follow the recent message put out by European Centre for Disease Prevention and Control (ECDC) reminding people to check their MMR status before travelling, to fully protect a community from the disease, including persons who have contraindications to the vaccine or who do not respond to the vaccine.

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Ethical approval

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Conflict of interest

No conflict of interest to declare.

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